

Attorney Docket No.: BD1 CIP FWC IV

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Sherie L. Morrison, et al.  
Serial No. : 08/266,154  
Filed : June 27, 1994  
For : RECEPTORS BY DNA SPLICING  
AND EXPRESSION  
Art Unit : 1806  
Examiner : Julie E. Reeves, Ph.D.

**OFFICIAL**#57/M  
1/10/97

November 6, 1997

Hon. Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

SECOND SUPPLEMENTAL AMENDMENT

Sir:

In accordance with the telephone interviews with the Examiner, kindly  
amend the application as follows:

IN THE TITLE

Please delete the current title and replace it with "Methods for Producing  
Functional Immunoglobulin, Including Chimeric Immunoglobulin, In Transformed  
Mammalian Lymphocytic Cells".

IN THE CLAIMS

78. (Three times amended) A method for producing a functional [antibody] immunoglobulin comprising a heavy chain and a light chain, which comprises the steps of:

(a) transfecting a [non-antibody producing] transformed mammalian [lymphoid] lymphocytic cell with a first DNA molecule coding for a first chain of the [antibody] immunoglobulin;

(b) transfecting the cell with a second DNA molecule, said second DNA molecule coding for a second chain of the [antibody] immunoglobulin, said second chain being a chain other than the first chain and said first and second chains being either the heavy chain or the light chain; and

(c) maintaining the cell in a nutrient medium, so that the cell expresses the first and second DNA molecules and the resultant chains are intracellularly assembled together to form the [antibody] immunoglobulin which is then secreted in a form capable of specifically binding to antigen[.]

wherein prior to step (a) the cell does not express a functional immunoglobulin capable of specifically binding antigen.

82. (Three times amended) A method as recited in claim 78 wherein prior to step (a) the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, [ which endogenously-produced heavy chain is not secreted in a form capable of specifically binding to antigen, ] but not both.

83. (Three times amended) A method as recited in claim 78 wherein the [antibody] immunoglobulin comprises the variable region found in a first mammalian species and comprises the constant region found in a second mammalian species, said second mammalian species being other than the first mammalian species.

84. (Three times amended) A method for producing a functional [antibody] immunoglobulin comprising a heavy chain and a light chain, which comprises the steps of:

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(a) transfecting a [non-antibody producing] transformed mammalian [lymphoid] lymphocytic cell with a plasmid comprising a first DNA molecule coding for a first chain of the [antibody] immunoglobulin and a second DNA molecule coding for a second chain of the [antibody] immunoglobulin, said second chain being a chain other than the first chain and said first and second chains being either the heavy chain or the light chain; and

(b) maintaining the cell in a nutrient medium so that the cell expresses said first DNA molecule and said second DNA molecule and the resultant chains are intracellularly assembled together to form the [antibody] immunoglobulin which is then secreted in a form capable of specifically binding to antigen[.]

wherein prior to step (a) the cell does not express a functional immunoglobulin capable of specifically binding antigen.

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88. (Three times amended) A method as recited in claim 84 wherein prior to step (a) the cell endogenously produces an immunoglobulin light chain or an

immunoglobulin heavy chain, [which endogenously-produced heavy chain is not secreted in a form capable of specifically binding to antigen,] but not both.

89. (Three times amended) A method as recited in claim 84 wherein the [antibody] immunoglobulin comprises the variable region found in a first mammalian species and comprises the constant region found in a second mammalian species, said second mammalian species being other than the first mammalian species.

90. (Three times amended) A method for producing a functional [antibody] immunoglobulin comprising a heavy chain and a light chain which comprises the steps of:

(a) maintaining in a nutrient medium a [non-endogenous antibody producing] transformed mammalian [lymphoid] lymphocytic cell, said cell having been transfected with a first DNA molecule coding for a first chain of the [antibody] immunoglobulin and a second DNA molecule coding for a second chain of the [antibody] immunoglobulin, said second chain being a chain other than the first chain and said first and second chains being either the heavy chain or the light chain;

(b) expressing from said cell the heavy chain and the light chain functionally assembled together to form said [antibody] immunoglobulin which is then secreted in a form capable of binding antigen; and

(c) recovering said [antibody.] immunoglobulin wherein prior to being transfected, the cell does not express a functional immunoglobulin capable of specifically binding antigen.

94. (Three times amended) A method as recited in claim 90 wherein prior to being transfected the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, [which endogenously-produced heavy chain is not secreted in a form capable of specifically binding to antigen,] but not both.

95. (Three times amended) A method as recited in claim 90 wherein the [antibody] immunoglobulin comprises the variable region found in a first mammalian source and comprises the constant region found in a second mammalian species, said second mammalian species being other than the first mammalian species.

#### REMARKS

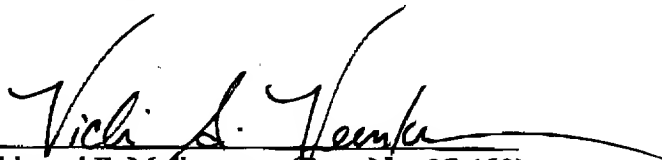
Applicants have amended the claims based on communications with the Examiner after submission of the Supplemental Amendment of August 28, 1997. While applicants believe they have enabled the practice of their invention in many non-lymphoid cells, applicants do not here pursue such claims in order to expedite issue of the pending claims. Similarly, the term "lymphoid", which does not appear in the specification, has been replaced with "transformed lymphocytic" because it is the adjective form of a term that does appear in the specification in the sentence on page 8, lines 32-36. As is clear from that statement in the specification, the term lymphocyte as used in this application includes myeloma and other lymphocytic plasma cells. Applicants have also changed "antibody" to "immunoglobulin" at the request of the examiner and believe that term to be at least as broad as antibody.

Applicants have not completed review of the Examiner's suggested claim renumbering, but undertake to do so promptly. Also in accordance with the Examiner's request, applicants will submit an amended abstract and recitation of the applications in the chain leading to the present application.

Applicants believe that the pending claims are now in condition for allowance. Entry of the present amendment and allowance of the claims are requested.

If the Examiner has any questions concerning this application, applicants request that the Examiner telephone the undersigned attorney at (415) 617-4011.

Respectfully submitted,



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Vicki S. Veenker

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Serial No. 08/266,154

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